

Applicants: Donghui Cui, et al.
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Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the following reference which is listed on the attached Form PTO-1449 (**Exhibit A**) and a copy of which is attached hereto as **Exhibit 1**:

1. U.S. Serial No. 09/873,746, filed June 4, 2001, Donghui Cui, et al. (**Exhibit 1**).

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the following disclosures which are listed on the attached Form PTO-1449 (**Exhibit A**) and which were previously submitted or cited in connection with the prosecution of U.S. Serial No. 09/873,746 from which the subject application claims priority under 35 U.S.C. §120. According to 37 C.F.R. § 1.98(d), copies of patents or publications that were previously cited by, or submitted to, the Patent Office in connection with such prior applications need not accompany the Information Disclosure Statement. Accordingly, copies of the following references are not attached to this Information Disclosure Statement.

1. U.S. Patent No. 4,438,117, issued March 20, 1984, Cherkofsky;
2. U.S. Patent No. 4,684,653, issued August 4, 1987, Taylor, et al.;
3. U.S. Patent No. 4,684,655, issued August 4, 1987, Atwal;
4. U.S. Patent No. 4,684,656, issued August 4, 1987, Atwal;

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5. U.S. Patent No. 4,703,120, issued October 27, 1987, J.B. Press;
6. U.S. Patent No. 4,728,652, issued March 1, 1988; Atwal;
7. U.S. Patent No. 4,845,216, issued July 4, 1989; Taylor, et al.;
8. U.S. Patent No. 4,855,301, issued August 8, 1989; Atwal, et al.;
9. U.S. Patent No. 4,882,334, issued November 21, 1989; Shih G., et al.;
10. U.S. Patent No. 4,902,796, issued February 20, 1990; Taylor, et al.;
11. U.S. Patent No. 4,946,846, issued August 7, 1990; Nomura, et al.;
12. U.S. Patent No. 5,134,145, issued August 28, 1992; Brouwer, et al.;
13. U.S. Patent No. 5,149,810, issued September 22, 1992; Perrior, et al.;
14. U.S. Patent No. 5,202,330, issued April 13, 1993; Atwal, et al.;
15. U.S. Patent No. 5,250,531, issued October 5, 1993; Cooper;
16. U.S. Patent No. 5,292,740, issued March 8, 1994; Burri, et al.;

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17. U.S. Patent No. 5,521,189, issued May 28, 1996; Boykin, et al.
18. U.S. Patent No. 5,541,186, issued July 30, 1996; Breu, et al.;
19. U.S. Patent No. 5,500,424, issued March 19, 1996; Nagamine, et al.;
20. U.S. Patent No. 5,594,141, issued January 14, 1997; Yuan, et al.;
21. U.S. Patent No. 5,942,517, issued August 24, 1999; Nagarathnam, et al.;
22. PCT International Publication No. WO 99/48530, published September 30, 1999;
23. PCT International Publication No. WO 99/07695, published February 18, 1999;
24. PCT International Publication No. WO 98/51311, published November 19, 1998;
25. PCT International Publication No. WO 97/42956, published November 20, 1997;
26. PCT International Publication No. WO 94/22829, published October 13, 1994;
27. PCT International Publication No. WO 94/10989, published May 26, 1994;

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28. PCT International Publication No. WO 92/14453, published September 3, 1992;
29. PCT International Publication No. WO 92/00741, published January 23, 1992;
30. European Patent Application No. 0 627 427, published December 7, 1994;
31. European Patent Application No. 0 622 369 published November 2, 1994;
32. European Patent Application No. 0 622 366, published November 2, 1994;
33. European Patent Application No. 0 459 666 published December 4, 1991;
34. European Patent Application No. 0 400 655, published December 5, 1990;
35. European Patent Application No. 0 280 227, published August 31, 1988;
36. European Patent Application No. 0 237 347 published September 16, 1987;
37. European Patent Application No. 0 236 902, published September 16, 1987;
38. European Patent Application No. 0 234 830, published September 2, 1987;

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39. European Patent Application No. 0 204 317, published December 10, 1986;
40. European Patent Application No. 0 162 208, published November 27, 1985;
41. French Application No. 2,610,625, August 12, 1988;
42. Japanese Patent Application No. 56-59778, May 23, 1981;
43. Japanese KOKAI 62-265271, November 18, 1987;
44. Japanese KOKAI No. 62-87574, April 22, 1987;
45. Japanese KOKAI 61-282367, December 12, 1986;
46. Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 2,3-Substituted-4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," *J. Med. Chem.* 33: 2629-2635 (1990);
47. Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 3,3-Carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Orally Effective Antihypertensive Agents," *J. Med. Chem.* 34: 806-811 (1991);
48. Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers: 2-Heterosubstituted 4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," *J. Med. Chem.* 33: 1510-1515 (1990);

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U.S. Serial No.: Not Yet Known

Filed: Herewith

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49. Atwal, et al., "Substituted 1,4-Dihydropyrimidines. 3. Synthesis of Selectively Functionalized 2-Hetero-1,4-dihydropyrimidines," *J. Org. Chem.* 54: 5898-5907 (1989);
50. Atwal, et al., "Synthesis of Substituted 1,2,3,4-Tetrahydro-6-Methyl-2-Thioxo-5-Pyrimidinecarboxylic Acid Esters," *Heterocycles* 26: 1189-1192 (1987);
51. Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 3.3-Carbamoyl-4-aryl-1,2,3,4-tetra-hydro-6-methyl-pyrimidene-carboxylic Acid Esters as Orally Effective Antihypertensive Agents," *J. Med. Chem.* 34(2):76-81 (1991);
52. Barrio, et al., "A Direct Method For Preparation of 2-Hydroxyethoxymethyl Derivatives of Guanine, Adenine, and Cytosine," *J. Med. Chem.* 23(5): 572-574 (1980);
53. Boer, et al., "(+)-Niguldipine binds with very high affinity to Ca^{2+} channels and to a subtype of adrenoceptors," *Eur. J. Pharm. - Mol. Pharm. Sec.* 172: 131-145 (1989);
54. Brown, et al., "Inhibitors of *Bacillus subtilis* DNA Polymerase III. 6-(Arylalkylamino)uracils and 6-Anilinouracils," *J. Med. Chem.* 20(9): 1186-1189 (1977);
55. Cho, et al., "Dihydropyrimidines: Novel Calcium Antagonists with Potent and Long-Lasting Vasodilative and Antihypertensive Activity," *J. Med. Chem.* 32: 2399-2406 (1989);
56. Cho, et al., "Regioselective Synthesis of N-Substituted

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U.S. Serial No.: Not Yet Known
Filed: Herewith
Page 15

- Dihydropyrimidin-2(1H) or (3H) - One," *Tetrahedron Ltrs* 29(42): 5405-5408 (1998);
57. D'Eletto and Javitt, "Effect of Doxazosin on Cholesterol Synthesis In Cell Culture," *J. Cardio. Pharm.*, 13(Supp.2): S1-S4 (1989);
58. Forray, et al., "The α_1 -Adrenergic Receptor That Mediates Smooth Muscle Contraction in Human Prostate Has the Pharmacological Properties of the Cloned Human α_1 Subtype," *Mol. Pharm.* 45: 703-708 (1994);
59. Khanina, E.L., et al., Alkylation of derivatives of 2-oxo-4-phenyl-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxlic acid. *Chem Abs.* 89: 43319 (1978);
60. Mamaev, V.P. and Dubovenko, ZD., Pyrimidines. XXI. 5-Substituted 2-hydroxy-4,6-diphenylpyrimidines. *Chem. Abs.* 73: 77187 (1970);
61. McGrath, et al., "Alpha-Adrenoceptors: A Critical Review," *Med. Res. Rev.*, 9(4): 407-533 (1989);
62. Rovnyak, et al., "Dihydropyrimidine Calcium Channel Blockers. 4. Basic 3-Substituted-4-aryl-1,4-dihydropyrimidine-5-carboxylic Acid Esters," *J. Med. Chem.* 35: 3254-3263 (1992);
63. Spiers, et al., "UK-52,046 (A Novel α_1 -Adrenoceptor Antagonist) and the Role of α_1 -Adrenoceptor Stimulation and Blockade on Atrioventricular Conduction," *J. Cardio. Pharm.*, 16: 824-830 (1990);

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64. Triggle, "Dihydropyrimidine Calcium Channel Blockers. 2,3-Substituted 4-Aryl-1,4-dihydro-6-methyl-5-pyrimidine-Carboxylic Acid Esters as Potent Mimics of Dihydropyridines," *Chemtracts. - Org. Chem.*, pg 68-72 (Jan/Feb 1991);
65. Wetzel, et al., "Discovery of α_1 -Adrenergic Receptor Antagonists Based on the L-Type Ca^{2+} Channel Antagonist Niguldipine," *J. Med. Chem.*, 38(10): 1579-1581 (1995);
66. Zhan, et al., "Bunazosin Reduces Intraocular Pressure By Increasing Uveoscleral Outflow In Rabbits," *Invest. Ophthal. and Visual Science*, 34: Abst. No. 1133-49, pg. 928 (1993);
67. PCT International Publication No. WO 96/14846, published May 23, 1996;
68. U.S. Patent No. 6,207,444, issued March, 2001, Sidler, et al.;
69. U.S. Patent No. 6,245,773, issued June, 2001, Wong, et al.;
70. U.S. Patent No. 6,268,369, issued July, 2001, Nagarathnam, et al.; and
71. U.S. Patent No. 6,274,585, issued August, 2001, Cui, et al.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee, other than the enclosed fee of \$806.00 for filing the subject application, is deemed necessary in connection with the filing of this Preliminary Amendment and Information Disclosure Statement. However, should any additional fee be found necessary, authorization is hereby given to charge such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
1795/57107-AAA/JPW/ANXSerial No.
Not Yet KnownINFORMATION DISCLOSURE CITATION
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Donghui Cui, et al.Filing Date:
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Group Art Unit

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number							Date	Name	Class	Subclass	Filing Date if Appropriate
	4	4	3	8	1	1	7	3/20/84	Cherkofsky			
	4	6	8	4	6	5	3	8/4/87	Taylor, et al.			
	4	6	8	4	6	5	5	8/4/87	Atwal			
	4	6	8	4	6	5	6	8/4/87	Atwal			
	4	7	0	3	1	2	0	10/27/87	J.B. Press			
	4	7	2	8	6	5	2	3/1/88	Atwal			
	4	8	4	5	2	1	6	7/4/89	Taylor			
	4	8	5	5	3	0	1	8/8/89	Atwal			
	4	8	8	2	3	3	4	11/21/89	Shih			
	4	9	0	2	7	9	6	2/20/90	Taylor			
	4	9	4	6	8	4	6	8/7/90	Nomura			
	5	1	3	4	1	4	5	8/28/92	Brouwer, et al.			
	5	1	4	9	8	1	0	9/22/92	Perrior, et al.			
	5	2	0	2	3	3	0	4/13/93	Atwal, et al.			
	5	2	5	0	5	3	1	10/5/93	Cooper			
	5	2	9	2	7	4	0	3/8/94	Burri, et al.			
	5	5	2	1	1	8	9	5/28/96	Boykin, et al.			
	5	5	4	1	1	8	6	7/30/96	Breu, et al.			
	5	5	0	0	4	2	4	3/19/96	Nagamine, et al.			
	5	5	9	4	1	4	1	1/14/97	Yuan, et al.			
	5	9	4	2	5	1	7	8/24/99	Nagarathnam, et al.			

FOREIGN PATENT DOCUMENTS

		Document Number							Date	Country	Class	Subclass	Translation		
													Yes	No	
	WO	9	9	4	8	5	3	0	9/30/99	PCT					
	WO	9	9	0	7	6	9	5	2/18/98	PCT					
	WO	9	8	5	1	3	1	1	11/19/98	PCT					
	WO	9	7	4	2	9	5	6	11/20/97	PCT					
	WO	9	4	2	2	8	2	9	10/13/94	PCT					
	WO	9	4	1	0	9	8	9	5/26/94	PCT					
	WO	9	2	1	4	4	5	3	9/3/92	PCT					
	WO	9	2	0	0	7	4	1	1/23/92	PCT					
		0	6	2	7	4	2	7	12/7/94	EPO					
		0	6	2	2	3	6	9	11/2/94	EPO					

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		0	6	2	11/2/94	EPO			Yes	No
		0	4	5	12/4/91	EPO				
		0	4	0	12/5/90	EPO				
		0	2	8	8/31/88	EPO				
		0	2	3	9/16/87	EPO				
		0	2	3	9/16/87	EPO				
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		2	6	1	8/12/88	France				
		5	6	5	5/23/81	Japan				
		6	2	2	11/18/87	Japanese-KOKAI				
		6	2	8	4/22/87	Japanese-KOKAI				
		6	1	2	12/12/86	Japanese-KOKAI				
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)										
		Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 2. 3-Substituted-4-aryl-1,4-dihydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Potent Mimics of Dihydropyridines," <i>J. Med. Chem.</i> . 33: 2629-2635 (1990);								
		Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 3. 3-Carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5-pyrimidinecarboxylic Acid Esters as Orally Effective Antihypertensive Agents," <i>J. Med. Chem.</i> . 34: 806-811 (1991);								
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		Atwal, et al., "Synthesis of Substituted 1,2,3,4-Tetrahydro-6-Methyl-2-Thioxo-5-Pyrimidinecarboxylic Acid Esters," <i>Heterocycles</i> 26: 1189-1192 (1987);								
		Atwal, et al., "Dihydropyrimidine Calcium Channel Blockers. 3 .3-Carbamoyl-4-aryl-1,2,3,4-tetra-hydro-6-methyl-pyrimidinecarboxylic Acid Esters as Orally Effective Antihypertensive Agents," <i>J. Med. Chem.</i> . 34(2):76-81 (1991)								
		Barrio, et al., "A Direct Method For Preparation of 2-Hydroxyethoxymethyl Derivatives of Guanine, Adenine, and Cytosine," <i>J. Med. Chem.</i> . 23(5): 572-574 (1980);								
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Boer, et al., "(+)-Niguldipine binds with very high affinity to Ca ²⁺ channels and to a subtype of α_1 -adrenoceptors," <i>Eur. J. Pharm. - Mol. Pharm.</i> , Sec. 172: 131-145 (1989);
	Brown, et al., "Inhibitors of <i>Bacillus subtilis</i> DNA Polymerase III. 6-(Arylalkylamino)uracils and 6-Anilinouracils," <i>J. Med. Chem.</i> 20(9): 1186-1189 (1977);
	Cho, et al., "Dihydropyrimidines: Novel Calcium Antagonists with Potent and Long-Lasting Vasodilative and Antihypertensive Activity," <i>J. Med. Chem.</i> 32: 2399-2406 (1989);
	Cho, et al., "Regioselective Synthesis of N-Substituted Dihydropyrimidin-2(1H) or (3H) - One," <i>Tetrahedron Ltrs</i> 29(42): 5405-5408 (1998);
	D'Eletto and Javitt, "Effect of Doxazosin on Cholesterol Synthesis In Cell Culture," <i>J. Cardio. Pharm.</i> , 13(Supp.2): S1-S4 (1989);
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	Wetzel, et al., "Discovery of α_{1a} -Adrenergic Receptor Antagonists Based on the L-Type Ca ²⁺ Channel Antagonist Niguldipine," <i>J. Med. Chem.</i> , 38(10): 1579-1581 (1995);
	Zhan, et al., "Bunazosin Reduces Intraocular Pressure By Increasing Uveoscleral Outflow In Rabbits," <i>Invest. Ophthal. and Visual Science</i> , 34: Abst. No. 1133-49, pg. 928 (1993)

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	US	6	2	0	7	4	4	03/01	Siderler, et al.			
	US	6	2	4	5	7	7	06/01	Wong, et al.			
	US	6	2	6	8	3	6	07/01	Nagarathnam, et al.			
	US	6	2	7	4	5	8	08/01	Cui, et al.			
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		9	6	1	4	8	4	6	05/23/96	PCT	Yes	No
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